

REMARKS

This amendment is submitted in an earnest effort to bring this application to issue without delay.

Applicants have withdrawn claims 9 through 13 and 21 through 24, withdrawn from further consideration, as directed to a non-elected invention. Applicants reserve the right to claim the non-elected subject matter in the canceled claims in a related application.

Applicants have amended claims 1 through 6 and 14 through 20 and added new claims 26 and 27 in order to more clearly define the invention and to more sharply focus on the nature of the invention. Antecedent basis for the amended claims and for the new claims may be found in the specification on page 4, last three lines, through page 11, line 7, and page 28, line 6 to the bottom, especially lines 21 through 25. Thus claims 1 through 8, 14 through 20, 26 and 27 are now in the application and are presented for examination.

In response to the objections to the claims on page 3 of the office action, Applicants have amended the claims to respond to the points raised by the Examiner with the exception of his complaint about the word "lesser". Applicants do not see anything wrong with use of the word "lesser" in the context of L-serine dehydratase expressed to a lesser degree. Applicants cite to the Examiner page 653 of the Webster's New Collegiate Dictionary (1981)

(copy enclosed) where "lesser" is defined as "of less size, quantity or significance." Here the extent of the expression of the L-serine dehydratase is of less quantity or significance and so Applicants have used the word "lesser" in a proper fashion.

In response to the rejection of the claims under 35 USC 112, second paragraph, as indefinite, as set forth on pages 4 and 5 of the office action, Applicants believe that the claims as now presented deal with all of the issues raised by the Examiner. Throughout the amended claims as attached, Applicants have deleted the expression "characterized in that." In claims 1 and 2, Applicants believe that the term "lesser" in "lesser extent" is not indefinite, but is entirely proper as has already explained in the preceding paragraph.

Applicants have also amended claims 1 and 2 to make it clear that the expression of the nucleotide sequence according to the invention is to a lesser degree than the expression of the naturally occurring L-serine dehydratase having a nucleotide sequence of Seq ID NO:1. Applicants have amended claim 1 to state that the polynucleotide sequence encoding L-serine dehydratase is partially or completely deleted or is mutated, or is expressed to a lesser degree than the expression of the naturally occurring L-serine dehydratase having nucleotide sequence of SEQ ID NO: 1 or which is not expressed at all. Applicants have amended claim 2, which is dependent upon claim 1, to state that the polynucleotide sequence encoding L-serine dehydratase is partially deleted or is mutated and expressed to a lesser extent in comparison with the

expression of the naturally occurring L-serine dehydratase having a nucleotide sequence of Seq ID NO:1 or not expressed at all. Antecedent basis for these changes may be found in the specification on page 5, line 14 through page 7, line 20, especially on page 5, lines 14 to 16, and page 6, lines 11 through 13 providing antecedent basis for deleting the entire L-serine dehydratase sequence (sdaA), all 1449 nucleotides, as included in claim 1.

On page 4 of the office action, lines 6 through 11 from the bottom, the Examiner has questioned how the entire L-serine dehydratase sequence (sdaA) can be completely deleted as there would be nothing left of the polynucleotide sequence on which the Applicants could perform recombinant technology. However, such is not the case. The recombinant nucleic acid according to the present invention includes first of all at least one serine biosynthesis sequence selected from the group consisting of serA, serB, and serC. It is the serine biosynthesis gene that is expressed to obtain the enzyme needed to convert carbohydrates such as glucose to L-serine. The L-serine dehydratase sequence is a naturally occurring polynucleotide that expresses an enzyme that degrades the L-serine to pyruvate. If this sequence is deleted in its entirety, then the L-serine will not be degraded at all, and the presently claimed recombinant nucleic acid contains only the polynucleotide sequence that expresses the enzyme needed to prepare L-serine, and does not contain at all the polynucleotide sequence that expresses L-serine dehydratase, which undesirably degrades the

L-serine to pyruvate. Such a recombinant nucleic acid will be valuable indeed.

In claim 3 last presented the Examiner has complained that the terms "homolog", "derivative", and "hybridizing conditions" are indefinite, and has rejected the claims under 35 USC 112, second paragraph. Applicants have amended claim 3 to define the homolog as having a sequence complementary to the nucleotide sequence, and have deleted the word "derivative" and have stated that the "hybridizing" takes place "under stringent conditions." Antecedent basis for these changes may be found in the specification in the paragraph bridging pp 10 and 11. Applicants have also included new claims 26 and 27, which define the nucleotide sequences of claim 3 even more sharply. In claims 14 and 15 Applicants have indicated that the expression of the recombinant L-serine dehydratase is to a reduced extent with respect to the naturally occurring L-serine dehydratase having SEQ ID NO: 1. Applicants have made changes in claims 16, 18 and 19 to delete the language to which the Examiner objects as not making any sense and have canceled claim 20. Applicants believe that all claims now presented are in full compliance with the requirements of 35 USC 112, second paragraph.

The Examiner has rejected claims 1 through 8, and 14 through 20 under 35 USC 112, first paragraph, as directed to subject matter that has not been adequately described in the specification. The Examiner further rejects the claims under the first paragraph of 35 USC 112, on the grounds that the

specification does not enable those "skilled in the art" to make and to use the present invention without the need to conduct undue experimentation. The Examiner argues that the specification does not disclose any form of L-serine dehydratase beyond the scope of the polynucleotide having SEQ ID NO: 1 where one or more residues from positions 506 to 918 are deleted. Applicants strongly disagree with both arguments under 35 USC 112, first paragraph.

Applicants have amended independent claim 1, and have explained in the remarks herein above, to make it clear that the polynucleotide sequence that expresses at least one serine biosynthesis sequence (serA, serB or serC) is the polynucleotide sequence that is needed to catalyze the conversion of a carbohydrate, such as glucose, to L-serine. The polynucleotide sequence L-serine dehydratase, which is also present as part of the recombinant nucleic acid for promoting microbial production of L-serine from the carbohydrates, is actually a factor that impedes obtaining the L-serine, because the expressed enzyme L-serine dehydratase facilitates the degradation of L-serine to pyruvate. Thus it is desirable to limit as much as possible the expression of the portion of the polynucleotide sequence that expresses L-serine dehydratase to prevent the undesired degradation of the L-serine dehydratase. The specification on page 6, line 11 through page 11, line 15 adequately defines the presently claimed recombinant nucleic acids, and adequately discloses how to make and how to use the presently claimed recombinant nucleic acids for promoting

microbial production of L-serine. Thus all claims now presented are believed to fully comply with the requirements of 35 USC 112.

The Examiner also questions in the central paragraph of page 6 of the what is the utility of the recombinant polynucleotide encoding L-serine dehydratase. Applicants have responded by amending the claims to make it clear that the utility of the recombinant polynucleotide encoding L-serine dehydratase is to promote microbial production of L-serine directly from carbohydrates by promoting expression of the also encoded nucleotide sequence expressing serA, serB and serC, and by avoiding or by at least reducing decomposition of the L-serine to pyruvate. Antecedent basis may be found in the specification (English language) in the paragraph bridging pp 3 and 4 and in the paragraph bridging pp 4 and 5. Thus all claims now presented comply with the description requirements and the enablement requirements of 35 USC 112, first paragraph.

The Examiner has rejected claims 1,2, 4 through 8, and 14 through 20, as last presented, under 35 USC 102(b) as anticipated by KUBOTA et al. The Examiner argues that KUBOTA et al discloses a mutant gene having a reduced sdaA activity and coryneform bacteria expressing said mutant gene. Applicants do not agree that KUBOTA et al anticipated under 35 USC 102 or renders obvious under 35 USC 103 any claim now presented. At the outset Applicants stress that KUBOTA et al discloses no structure of the polynucleotide sequence expressing L-serine dehydratase, nor any disclosure of how to specifically disclose the expression of the sequence. The

reference discloses undirected mutagenesis methods to increase the production of L-serine and to reduce the activity of the L-serine-dehydratase by 32%.

According to KUBOTA et al the cellular activity of L-serine dehydratase, which is responsible for the undesired L-serine degradation, is decreased. As a result, the L-serine concentration in *Corynebacterium glycinophilum* will be reduced. This perception is a result of various experiences including undirected mutagenesis methods. Because the method of mutagenesis are undirected there is no knowledge about the reason why the L-serine production is increased. The best results which were obtained by KUBOTA et al are a reduction in the activity of the L-serine dehydratase by 32%.

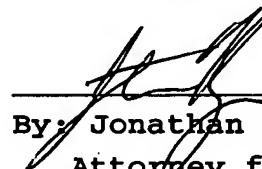
Contrary to KUBOTA et al, Applicants have found the entire structure of the L-serine dehydratase gene, entirely responsible for the *sdaA* production. As a result Applicants are able to minimize or completely deactivate the activity of L-serine dehydratase by an action that is not accidental, but directed. In KUBOTA et al there is no disclosure of how to find the polynucleotide sequence which is able to control the expression of L-serine dehydratase, and there is also no sequence given. Thus Applicants believe that KUBOTA et al provides no basis to reject any claim now presented as anticipated under 35 USC 102 or as obvious under 35 USC 103.

Applicants would like to schedule a telephone interview with the Examiner to discuss the claims in this case and the KUBOTA et al reference, once he has had a chance to consider the Applicants' response.

Applicants believe that all claims now presented are in condition for allowance and a response to that effect is earnestly solicited. Applicants are enclosing a petition to obtain a one month extension of the term for response and PTO Form 2038, completed, to enable the undersigned to charge the cost of obtaining the extension to their credit card.

Respectfully submitted,

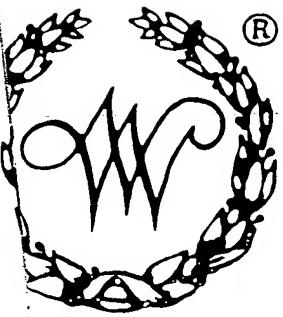
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Lepcha ○ letdown

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prp. of *lenire* to
1 : exerting a
less 2 : of mild
SOFT *ant* cau-

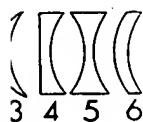
jen-ē-lēn-ə-pē.

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in due is ~, ~

us, fr. L *lenitus*,
HUNG — lenitive

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see MERCY *ant*



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o-concave, 5 bi-con-
verging meniscus

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fr. *lento* slow]

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: lens, lens lentil]

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de with lenticules

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on, *leo*] : of, relat-



(ana *pipiens*) that is
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utheastern U.S.
T. Aerial gymnast]
s, a high neck, and

ankle-length legs worn for practice or performance by dancers, acrobats, and aerialists; also : TIGHTS
Lepcha \lep-chə\ n, pl Lepcha or Lepchas 1 : a member of a Mongoloid people of Sikkim, India 2 : the Tibeto-Burman language of the Lepcha people
lep-or \lep-ər\ n [ME, fr. *lepre* leprosy, fr. OF, fr. LL *lepra*, fr. Gk, fr. *lepein* to peel; akin to OĒ *lefer* reed] 1 : a person affected with leprosy 2 : a person shunned for moral or social reasons : OUT-CAST
lepid- or lepido- comb form [NL, fr. Gk, fr. *lepid*, *lepis* scale, fr. *lepein*] : flake; scale (Lepidoptera)
lepidolite \li-pid'ə-lit\ n [G *lepidolith*, fr. *lepid*- + *olith*] : a variable mineral typically K (Li, Al) (Si, Al)O₁₀ (F, OH)₂ that consists of a mica containing lithium and is used esp. in glazes and enamels
lepidopteran \lep-ə-däp-tə-rən\ n [NL *Lepidoptera* order of insects, fr. *lepid*- + Gk *pteron* wing — more at FEATHER] : any of a large order (Lepidoptera) of insects comprising the butterflies, moths, and skippers that as adults have four broad or lanceolate wings usu. covered with minute overlapping and often brightly colored scales and that as larvae are caterpillars — lepidopteran adj — lepidopterous \lep-ə-tərəs\ adj

lepidopterist \lep-ə-tər-ist\ n : a specialist in lepidopterology
lepidopterology \lep-ə-tə-rə-ol'ə-jē\ n : a branch of entomology concerned with lepidopterans — lepidopterological \lep-ə-tərə-lōj'ik\ adj — lepidopterologist \lep-ə-tər-ol'ə-gist\ n
lepidopteron \lep-ə-däp-tə-rən\ n [NL, sing. of *Lepidoptera*] : LEPIDOPTERAN
lepidocyst \lep-ə-dō-sēt\ n, pl -do-cysts \-sēt\ [NL] : the arrangement and character of scales or shields (as on a snake)
lepidote \lep-ə-dōt\ adj [Gk *lepidōtēs* scaly, fr. *lepid*, *lepis*] : covered with scurfy scales (as rhododendrons)
leprechaun \lep-ro-kān', -kōn\ n [IrGael *leipreachán*] : a mischievous elf of Irish folklore usu. believed to reveal the hiding place of treasure if caught
leprosarium \lep-ro-sär-ē-ərē-əm\ n, pl -tums or -ia \-ē-ə\ [ML, fr. LL *leprosarium*] : a hospital for leprosy patients
leprosy \lep-ro-sē\ n [leprous + -y] 1 : a chronic disease caused by a bacillus (*Mycobacterium leprae*) and characterized by the formation of nodules or of macules that enlarge and spread accompanied by loss of sensation with eventual paralysis, wasting of muscle, and production of deformities and mutilations 2 : a morally or spiritually harmful influence (the ~ of poverty) — leprotic \lep-prō-tik\ adj

leprosy \lep-rō\ adj [ME, fr. LL *leprosus* leprous, fr. *lepra* leprosy] 1 a : infected with leprosy b : of, relating to, or resembling leprosy or a leper 2 : SCURVY — leprosely adv — leprosous \-sōs\ n
lepto- \lep-sē\ n comb form [MF *-lepsie*, fr. LL *-lepsia*, fr. Gk *-lepsia*, fr. *lepsis* fr. *lambanein* to take, seize — more at LATCH] : taking; seizure (*lympholepsy*)
leptocephalo- \lep-tə-kēfə-lō\ n, pl -li \-lē, -lē\ [NL, fr. Gk *lepis* + *kephalē* head — more at CEPHALIC] : a long thin small-headed transparent pelagic first larva of various eels
lepton \lep-tōn\ n, pl lepto- \-tō\ [NGk, fr. Gk, a small coin, fr. neut. of *leptos* peeled, slender, small] fr. *lepein* to peel — more at LEPER] — see *drachma* at MONEY table
lepton \lep-tōn\ n [Gk *leptos* + E *-on*] : any of a group of particles consisting of electrons, muons, and neutrinos that experience no strong interactions and are less massive than mesons and baryons — lepton-ic \lep-tōn-ik\ adj
lepto-osome \lep-tō-sōm\ adj [Gk *leptos* slender + *sōma* body] : ASTHENIC 2, ECTOMORPHIC — leptosome n
leptospire \-spīr\ n [NL *Lepthyspira*, genus name, fr. Gk *leptos* + *spira* coil — more at SPIRE] : any of a genus (*Lepthyspira*) of slender aerobic spirochetes that are free-living or parasitic in mammals — lepto-spiro-ail \lep-tə-spi-rō-ēl\ adj
lepto-spiro-ail \lep-tə-spi-rō-ēl\ n, pl -ro-ails \-sēl\ [NL] : any of several diseases of man and domestic animals that are caused by infection with leptospires
lepto-tene \lep-tō-tēn\ [ISV] : a stage of meiotic prophase immediately preceding synapsis in which the chromosomes appear as fine discrete threads — leptotene adj

lepto-bi-an \lē-bē-ən\ adj, often cap 1 : of or relating to Lesbos 2 [fr. the reputed homosexual band associated with Sappho of Lesbos] : or relating to homosexuality between females

lebian \-bi-an\ adj, often cap : a female homosexual
lebi-bi-ism \lē-bē-bē-izm\ n : female homosexuality
lese majesty or lēse mā-jē-tē \lēz-ē-maj-ē-stē\ n [MF *lese majesté*, fr. L *laesa* *majestas*, lit., injured majesty] 1 a : a crime (as treason) committed against a sovereign power b : an offense violating the dignity of a ruler as the representative of a sovereign power 2 : a dereliction from or affront to dignity or importance
le-ction \lē-zhōn\ n [ME, fr. MF, fr. L *laesio*, *laesio*, fr. *laesus*, pp. of *laedere* to injure] 1 : INJURY, HARM 2 : an abnormal change in structure of an organ or part due to injury or disease; esp : one that is circumscribed and well defined

le-ped-e-za \lē-pō-dē-zə\ n [NL, irreg. fr. V. M. de Zepedas 1785 Sp governor of East Florida] : any of a genus (*Leptezeda*) of herbaceous or shrubby leguminous plants including some widely used for forage, soil improvement, and esp. hay
less \lēs\ adj [ME, partly fr. OE *lēs*, adv. & n.; partly fr. *lēssa*, adj.; akin to OFris *lēs* less, Gk *lēmē* hunger] 1 : constituting a more limited number (~ than three) 2 : of lower rank, degree, or importance (no ~ a person than the president himself) 3 a : of reduced size, extent, or degree b : more limited in quantity (in ~ time)

syn LESS, LESSER, SMALLER, FEWER shared meaning element : not as great (as in size, number, worth, or significance) as some expressed or implied other. In spite of the common element of meaning these terms are rarely interchangeable without loss of precision. LESS is its most characteristic use applies to matters of degree, value, or amount, is opposed to *more*, and chiefly modifies collective nouns or nouns denoting a mass or an abstract whole (the moon gives less light than the sun) Less is sometimes applied

to matters of number, but the usage is decried by many careful writers and speakers. LESSER applies especially to matters of quality, worth, or significance and is opposed to *greater* or *major* (God made . . . the lesser light to rule the night — Gen 1:16 (AV)) In vernacular names of plants and animals lesser specifically implies distinction based on relative smallness (the lesser yellowlegs) (lesser celandine) SMALLER is applicable especially to matters of size, dimension, or quantity and is opposed to *larger* (the advantage of *smaller cars*) (use a *smaller amount of seasoning*) FEWER applies specifically to matters of number and therefore regularly modifies a plural noun. Thus, "he has *fewer* (not *less*) spendable dollars this year," but "he has *less* (not *fewer*) money to spend than he used to." Occasionally the distinction between quantity and number is obscured and either *fewer* or *less* is appropriate (seasonal workers who average *fewer* (or *less*) than six months' work a year) *ant* more

2 less *adv* : to a lesser extent or degree — less and less : to a progressively smaller size or extent — less than : by no means : not at all (was being less honest in his replies)

3 less *prep* : diminished by : MINUS

4 less n, pl less 1 : a smaller portion or quantity 2 : something of less importance

5 less \lēs\ adj suffix [ME *-les*, -lese, fr. OE *lēas* devoid, false; akin to OHG *lās* loose, OE *lesian* to get lost — more at LOSE] 1 : destitute of : not having (witness) (childless) 2 : unable to be acted on or to act (in a specified way) (dauntless) (fadedless)

6 less-ee \lēs-ē\ n [ME, fr. AF, fr. *lēs* pp. of *lesse* to lease — more at LEASE] : one that holds real or personal property under a lease less-ee-en \lēs-n\ less-ened; lessening \lēs-niŋ, -n-ē\ vi : to shrink in size, number, or degree : DECREASE ~ vi 1 : to reduce in size, extent, or degree 2 a archaic : to represent as of little value : MINIMIZE b : to lower in status or dignity : DEGRADE syn see DECREASE

7 less-er \lēs-ər\ adj : of less size, quality, or significance syn see LESS, *ant* greater, major

8 less-er *adv* : LESS (lesser-known)

lesser Bear n : URSA MINOR

lesser celandine n : CELANDINE 2

lesser cornstalk borer n : a pyralid moth (*Elasmopalpus lignosellus*) whose slender greenish larva is a destructive pest that burrows in the stalk esp. of Indian corn near ground level

lesser Dog n : CANIS MINOR

lesser peach tree borer n : a moth (*Synanthedon pictipes* family Aegeridae) whose larva is a borer in the forks and crotches of stone-fruit trees and esp. the peach

lesser scaup n : a common No. American diving duck (*Aythya affinis*) similar to but smaller than the greater scaup with a purplish iridescence on the head of the adult male — called also lesser scaup duck

lesser yellowlegs n pl but sing or pl in constr : a common American marsh and shore bird (*Tringa flavipes*) that closely resembles the greater yellowlegs in color and markings but is smaller with a shorter more slender bill

les-son \lēs-ən\ n [ME, fr. OF *lesson*, fr. LL *lectio*, *lectio*, fr. L, act of reading, fr. *lectus* pp. of *legerē* to read — more at LEGEND] 1 : a passage from sacred writings read in a service of worship 2 a : a piece of instruction : TEACHING b : a reading or exercise to be studied by a pupil c : a division of a course of instruction 3 a : something learned by study or experience (his years of travel had taught him valuable ~s) b : an instructive example (the ~s history has for us) c : REPRIMAND

2 lesson vt less-soned: less-soning \lēs-ə-niŋ, lēs-niŋ\ 1 : to give a lesson to : INSTRUCT 2 : LECTURE, REBUKE

les-son \lēs-ən\ n [ME *lesson*, fr. AF, fr. *lesse* to lease] : one that conveys property by lease

lest \lēst\ conj [ME *les* the, *lest*, fr. OE *lēs* the, fr. *thē* (instrumental of that that) + *lēs* + the, the relative particle] : for fear that — used after an expression denoting fear or apprehension (worried ~ he should be late) (hesitant to speak out ~ he be branded a troublemaker)

let \lēt\ vt let-ted; letted or let; let-ting [ME *letten*, fr. OE *lētan* to delay, hinder; akin to OHG *lēzzan* to permit, L *lēs* weary, *lēs* soft, mild] vt 1 : to cause to : ~ it be known 2 a : to offer or grant for rent or lease (~ rooms) b : to assign esp. after bids (~ a contract) 3 a : to give opportunity to whether by positive action or by failure to prevent (live and ~ live) (a break in the clouds ~ him see his objective) b : used in the imperative to introduce a request or proposal (~ us pray) c : used as an auxiliary to express a warning (~ him try)

4 : to free from or as if from confinement : RELEASE (~ the prisoner go) (she ~ out a scream) 5 : to permit to enter, pass, or leave (~ them through) ~ vi 1 : to become rented or leased 2 : to become awarded to a contractor

gyn 1 see HIRE

2 LET, ALLOW, PERMIT, SUFFER shared meaning element : to neither forbid nor prevent

let \lēt\ n suffix [ME, fr. MF *-lēt*, -el, dim. suffix (fr. L *-ellus*) + *-et*] 1 : small one (booklet) 2 : article worn on (wristlet)

let alone prep : to say nothing of : not to mention (lacked the courage, let alone the skill, to be effective)

let-down \lēt-dāw\ n 1 a : DISCOURAGEMENT, DISAPPOINTMENT

b : a slackening of effort : RELAXATION 2 : the descent of an air-

a abut * kitten or further a back a bake a cot, cart
nā out ch chin e less ē easy g gift i trip l life
j joke j sing ò flow ò flaw òi coin th thin th th
ü loot ü foot y yet yü few yü furious zh vision